



The Periodontal Cardiac Connection

Lieutenant Commander Jennifer L. Ellis, DC, USN and Captain John Mumford, DC, USN

Introduction

Over the last 10-15 years, a number of studies have been published suggesting a relationship between periodontitis and cardiovascular disease (CVD). Firstly, they have shown statistical associations between these two disease processes. Secondly, they have increased our understanding of common biological mechanisms that link the two disease processes. Thirdly, research has demonstrated that the treatment of periodontal disease can reduce risks of CVD events. In 2009, the editors of the American Journal of Cardiology and the Journal of Periodontology released a consensus paper to provide a better understanding of the links between periodontitis and atherosclerotic cardiovascular disease as well as providing an approach to reduce the risk of CVD events in patients with periodontitis (1). The purpose of this clinical update is to present the findings and recommendations put forth by the consensus paper between the periodontal and cardiac communities.(1)

Periodontitis and Atherosclerotic Cardiovascular Disease

Many, though not all, of the studies show a statistically significant association between the two diseases even after controlling for shared risk factors. A meta-analysis of studies linking periodontitis and coronary artery disease (CAD) by Humphrey, et al. determined that periodontitis is a separate risk factor from those traditionally associated with CAD and found a relative increased risk for CAD events in those with periodontitis ranging from 24% - 35% (3). This was in agreement with another meta-analysis by Bahekar et al. which found increased prevalence and incidence of CAD in patients with periodontitis (4). Both analyses concluded that further studies are indicated to clarify the relationship. A 2008 Veterans Affairs study by Dietrich et al. showed that men under the age of 60 with periodontal disease have twice the risk of developing CAD (5). Data from both NHANES I and the NHANES Follow-Up Study as well as the Health Professionals Follow-Up Study showed that periodontal disease and fewer teeth at baseline were associated with increased risk for cerebrovascular disease (6,7).

Mechanisms for Association between Periodontitis and Atherosclerotic CVD

It remains uncertain whether there is a cause and effect relationship between the two conditions. However, the immune system seems to be the common link between these disease processes. Inflammatory mediators released by the immune system are now understood to be associated with healing response, fighting disease, and more recently, they have been identified as active participants in developing diseases. Studies suggest two proposed biologic mechanisms that could support a direct link between periodontitis and atherosclerotic CVD. The first proposed mechanism is as an inflammatory disease. Moderate to severe periodontitis increases the overall level of systemic inflammatory mediators such as high sensitivity C reactive protein

(hsCRP), IL-6, and TNF- α (8,9). These inflammatory mediators in turn, are associated with CVD. Studies by de Beer in 1982 and Berk in 1990 showed higher quantiles of CRP predict future acute MI and Unstable Angina Pectoris (10,11). IL-6 and TNF- α are frequently abnormal in patients with acute coronary syndromes (12,13). The second proposed mechanism is the effects of associated periodontal pathogens. In untreated periodontitis there are 10^8 - 10^{12} gram negative bacteria adjacent to ulcerated gingival epithelium allowing an avenue of access to the systemic blood stream. Experimental models have shown periodontal pathogens promote platelet aggregation (14), foam cell formation (15), and development of atheromas (16,17). Further evidence giving plausibility to the second proposed mechanism was demonstrated by Harazthy et al. (18) who found gram negative bacteria normally associated with periodontal pockets within carotid artery atheromas.

In addition to the idea of a direct link between the two diseases, an indirect relationship between periodontitis and atherosclerotic CVD is seen in their many shared risk factors such as smoking, diabetes mellitus, obesity, elevated lipids, and potentially hypertension. These shared risk factors can blur the connection between the two though statistical analysis attempts to control for these confounding factors. Systemic inflammation is the common underlying feature shared by all of these conditions including periodontitis and CVD.

Treatment of Periodontitis

It has been established that treatment of periodontitis can reduce the common systemic inflammatory mediators associated with periodontitis and CVD potentially reducing the risk of CVD events. Paraskevas et al. and Tonetti et al. (19,20) demonstrated periodontal therapy decreased the level of CRP, IL-6 and other systemic inflammatory mediators giving credence to the first theory. In addition, treatment of periodontitis removes the bacterial biofilm attached to the tooth roots and results in reduction of the clinical signs of disease and bacterial load. This has the potential to reduce future bacteremias and the development of atheromas.

Recommendations for patients with periodontitis (1)

- 1) Inform patients with moderate to severe periodontitis that their oral condition may put them at increased risk for atherosclerotic CVD. If the patient also has a major cardiac risk factor such as hypertension, smoking, or diabetes they should be informed that getting a physical evaluation within the year is advisable. For patients with 2 or more cardiac risk factors, the dental provider is encouraged to refer the patient to their physician for a physical evaluation.
- 2) Patients with periodontitis should receive a medical evaluation to assess their risk for atherosclerotic CVD, get a complete physical and annual measurement of their blood pressure. These

patients should also have a blood lipid profile and blood glucose measurement.

3) Periodontitis patients with abnormal lipid levels are encouraged to make lifestyle changes and may require medications as determined by their physician.

4) Smokers should be encouraged to quit smoking. If required, they should be given the resources to facilitate their attempt to quit.

5) Periodontal patients with hypertension should be treated to achieve target blood pressure (BP) levels according to the current JNC-7 guidelines through lifestyle changes and/or antihypertensive medications as determined by their physician.

Recommendations for patients with atherosclerotic CVD with or without a previous diagnosis of periodontitis (1)

The following recommendations are for the medical providers of patients with atherosclerotic CVD:

1) For patients with a previous diagnosis of periodontitis, it is recommended that there be a cooperative effort between the patient's physician and periodontist to optimize CVD risk reduction and periodontal care.

2) For those CVD patients who do not have an existing diagnosis of periodontitis, a periodontal evaluation should be completed for patients with gingival disease, unexplained tooth loss, or unexplained elevations of hsCRP or other inflammatory biomarkers.

3) For patients with untreated or uncontrolled periodontitis, a periodontal evaluation should be performed and treatment should be focused on controlling bacterial accumulations and eliminating inflammation.

Conclusion

Research continues to define the relationship between oral disease and systemic disease. Based on the work already completed, it is evident that there is a connection between periodontitis and atherosclerotic CVD. By identifying and treating periodontal disease, we may help reduce a patient's risk for a cardiac event.

References

1. Friedewald VE, Kornman KS, Beck JD, Genco R, Goldfine A, Libby P, Offenbacher S, Ridker PM, Van Dyke TE, Roberts WC. The American Journal of Cardiology and Journal of Periodontology Editors' Consensus: Periodontitis and Atherosclerotic Cardiovascular Disease. *J Periodontol* 2009 Jul;80: 1021-1032.
2. DeNardin, E. The Role of Inflammatory and Immunological Mediators in Periodontitis and Cardiovascular Disease. *Ann Periodontol* 2001;6: 30-40.
3. Humphrey LL, Fu R, Buckley DI, Freeman M, Helfand MJ. Periodontal disease and coronary heart disease incidence: A systematic review and meta-analysis. *J Gen Intern Med* 2008;23:2079-2086.
4. Bahekar AA, Singh S, Saha S, Molnar J, Arora R. The prevalence and incidence of coronary heart disease is significantly increased in periodontitis; A meta-analysis. *Am Heart J* 2007; 154: 830-837.
5. Dietrich T, Jimenez M, Krall Kaye EA, Vokonas PS, Garcia RI. Age-dependent associations between chronic

periodontitis/edentulism and risk of coronary heart disease. *Circulation* 2008;117:1668-1674.

6. Wu T, Trevisan M, Genco RJ, Dorn JP, Falkner KL, Sempos CT. Periodontal disease and risk of cerebrovascular disease: The First National Health and Nutrition Examination Survey and its follow-up study. *Arch Intern Med* 2000;160:2749-2755.

7. JSHIPURA KJ, Hung HC, Rimm EB, Willett WC, Ascherio A. Periodontal disease, tooth loss, and incidence of ischemic stroke. *Stroke* 2003;34: 47-52.

8. Wu T, Trevisan M, Genco R, Falkner K, Dorn J, Sempos C. Examination of the Relation between Periodontal Health Status and Cardiovascular Risk Factors: Serum Total and High Density Lipoprotein Cholesterol, C-reactive Protein, and Plasma Fibrinogen. *Am J Epidemiol* 2000; 151:273-82.

9. Loos B, Craandijk J, Hoek F, Wertheim-van Dillen P, van der Velden U. Elevation of Systemic Markers Related to Cardiovascular Diseases in the Peripheral Blood of Periodontitis Patients. *J Periodontol* 2000;71:1528-1534.

10. de Beer FC, Hind CRK, Fox KM, Allan RM, Maseri, Pepys MB. Measurement of C-reactive protein concentration in myocardial ischaemia and infarction. *Br Heart J* 1982; 47: 239-43.

11. Berk BC, Weintraub WS, Alexander RW. Elevation of C-reactive protein in "active" coronary artery disease. *Am J Cardiol* 1990;65(3):168-72.

12. Armstrong EJ, Morrow DA, Sabatine MS. Inflammatory biomarkers in acute coronary syndromes: Part I: Introduction and cytokines. *Circulation* 2006;113:e72-e75.

13. Inoue T, Komoda H, Nonaka M, Kameda M, Uchida T, Node K. Interleukin-8 as an independent predictor of long-term clinical outcome in patients with coronary artery disease. *Int J Cardiol* 2008;124:319-325.

14. Herzberg MC, Meyer MW. Dental Plaque, Platelets and Cardiovascular Diseases. *Ann Periodontol* 1998;3:151-160.

15. Qi M. Porphyromonas gingivalis induces murine macrophag foam cell formation. *Microb Pathog.* 2003; 35(6):259-67.

16. Lalla E, Lamster IB, Hofmann MA, Bucciarelli L, Jerud AP, Tucker S, Lu Y, Papapanou PN, Schmidt AM. Oral Infection With a Periodontal Pathogen Accelerates Early Atherosclerosis in Apolipoprotein E-Null Mice. *Arterioscler Thromb Vasc Biol.* 2003;23:1405-1411.

17. Li L, Messas E, Batista EL, Levine RA, Amar S. Porphyromonas gingivalis Infection Accelerates the Progression of Atherosclerosis in a Heterozygous Apolipoprotein E-Deficient Murine Model. *Circulation.* 2002;105:861-867.

18. Harazthy VI, Zambon JJ, Trevisan M, Zeid M, Genco RJ. Identification of periodontal pathogens in atheromatous plaques. *J Periodontol* 2008;71:1554-1560.

19. Paraskevas S, Huizinga JD, Loos BG. A systematic review and meta-analyses on C-reactive protein in relation to periodontitis. *J Clin Periodontol* 2008;35:277-290.

20. Tonetti MS, D'Aiuto F, Nibali L et al. Treatment of periodontitis and endothelial function. *N Engl J Med* 2007; 356:911-920.

Lieutenant Commander Ellis is a third year resident in the Periodontics Department at the Naval Postgraduate Dental School.

Captain Mumford is the Chairman of the Periodontics Department at the Naval Postgraduate Dental School.

The opinions and assertions contained in this article are the private ones of the authors and are not to be construed as official or reflecting the views of the Department of the Navy.

